

WHAT IS CLAIMED IS:

1. A human EPO receptor agonist polypeptide,
comprising a modified EPO amino acid sequence of the
5 Formula:

AlaProProArgLeuIleCysAspSerArgValLeuGluArgTyrLeuLeuGluAlaLys
10 GluAlaGluAsnIleThrThrGlyCysAlaGluHisCysSerLeuAsnGluAsnIleThr
ValProAspThrLysValAsnPheTyrAlaTrpLysArgMetGluValGlyGlnGlnAla
15 ValGluValTrpGlnGlyLeuAlaLeuLeuSerGluAlaValLeuArgGlyGlnAlaLeu
LeuValAsnSerSerGlnProTrpGluProLeuGlnLeuHisValAspLysAlaValSer
20 GlyLeuArgSerLeuThrThrLeuLeuArgAlaLeuGlyAlaGlnLysGluAlaIleSer
ProProAspAlaAlaSerAlaAlaProLeuArgThrIleThrAlaAspThrPheArgLys
25 LeuPheArgValTyrSerAsnPheLeuArgGlyLysLeuLysLeuTyrThrGlyGluAla
CysArgThrGlyAspArg SEQ ID NO:121
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wherein optionally 1-6 amino acids from the N-
35 terminus and 1-5 from the C-terminus can be deleted
from said EPO receptor agonist polypeptide;

wherein the N-terminus is joined to the C-terminus
directly or through a linker capable of joining the
40 N-terminus to the C-terminus and having new C- and N-
termini at amino acids;

23-24	48-49	111-112
24-25	50-51	112-113
25-26	51-52	113-114
26-27	52-53	114-115
27-28	53-54	115-116
28-29	54-55	116-117
29-30	55-56	117-118
30-31	56-57	118-119

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31-32	57-58	119-120
32-33	77-78	120-121
33-34	78-79	121-122
34-35	79-80	122-123
35-36	80-81	123-124
36-37	81-82	124-125
37-38	82-83	125-126
38-39	84-85	126-127
40-41	85-86	127-128
41-42	86-87	128-129
43-44	87-88	129-130
44-45	88-89	130-131
45-46	108-109	131-132
46-47	109-110	respectively; and
47-48	110-111	

said EPO receptor agonist polypeptide may optionally be immediately preceded by (methionine⁻¹), (alanine⁻¹) or (methionine⁻², alanine⁻¹).

5

2. The EPO receptor agonist polypeptide, as recited in claim 1, wherein said linker is selected from the group consisting of;

10

GlyGlyGlySer SEQ ID NO:123;

GlyGlyGlySerGlyGlyGlySer SEQ ID NO:124;

GlyGlyGlySerGlyGlyGlySerGlyGlyGlySer SEQ ID

NO: 125;

SerGlyGlySerGlyGlySer SEQ ID NO:126;

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GluPheGlyAsnMet SEQ ID NO:127;

GluPheGlyGlyAsnMet \ SEQ ID NO:128;

GluPheGlyGlyAsnGlyGlyAsnMet SEQ ID NO:129; and

GlyGlySerAspMetAlaGly \SEQ ID NO:130.

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3. The EPO receptor agonist polypeptide of claim 1 selected from the group consisting of;

SEQ ID NO:1; SEQ ID NO:2; \ SEQ ID NO:3; SEQ ID

NO:4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7;

SEQ ID NO:8; SEQ ID NO:9; SEQ ID NO:10; SEQ ID

25

NO:11; SEQ ID NO:12; SEQ ID NO:13; SEQ ID

NO:14; SEO ID NO:15; SEO ID NO:16; SEO ID

NO:17; SEQ ID NO:18; SEQ ID NO:19; SEQ ID

NO:20; SEQ ID NO:21; SEQ ID NO:22; SEQ ID

NO:23; SEQ ID NO:24; SEQ ID NO:25; \ SEQ ID

NO:26; SEQ ID NO:27; SEQ ID NO:28; SEQ ID
 NO:29; SEQ ID NO:30; SEQ ID NO:31; SEQ ID
 NO:32; SEQ ID NO:33; SEQ ID NO:34; SEQ ID
 NO:35; SEQ ID NO:36; SEQ ID NO:37; SEQ ID
 NO:38; SEQ ID NO:39; SEQ ID NO:40; SEQ ID
 NO:41; SEQ ID NO:42; SEQ ID NO:43; SEQ ID
 NO:44; SEQ ID NO:45; SEQ ID NO:46; SEQ ID
 NO:47; SEQ ID NO:48; SEQ ID NO:49; SEQ ID
 NO:50; SEQ ID NO:51; SEQ ID NO:52; SEQ ID
 NO:53; SEQ ID NO:54; SEQ ID NO:55; SEQ ID
 NO:56; SEQ ID NO:57; SEQ ID NO:58; SEQ ID
 NO:59 and SEQ ID NO:122.

4. The EPO receptor agonist polypeptide of
 claim 3 wherein the linker sequence (GlyGlyGlyGlySer
 SEQ ID NO:123) is replaced by a linker sequence
 selected from the group consisting of;

GlyGlyGlySerGlyGlyGlySer SEQ ID NO:124;

GlyGlyGlySerGlyGlyGlySerGlyGlyGlySer SEQ ID
 NO:125;

SerGlyGlySerGlyGlySer SEQ ID NO:126;

GluPheGlyAsnMet SEQ ID NO:127;

GluPheGlyGlyAsnMet SEQ ID NO:128;

GluPheGlyGlyAsnGlyGlyAsnMet SEQ ID NO:129; and
 GlyGlySerAspMetAlaGly SEQ ID NO:130.

5. A nucleic acid molecule comprising a DNA
 sequence encoding the EPO receptor agonist
 polypeptide of claim 1.

6. A nucleic acid molecule comprising a DNA
 sequence encoding the EPO receptor agonist
 polypeptide of claim 2.

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 "D1" and other initials below it.

7. A nucleic acid molecule comprising a DNA sequence encoding the EPO receptor agonist polypeptide of claim 3.

5 8. A nucleic acid molecule comprising a DNA sequence encoding the EPO receptor agonist polypeptide of claim 3 selected from the group consisting of;

10 SEQ ID NO:60; SEQ ID NO:61; SEQ ID NO:62; SEQ ID NO:63; SEQ ID NO:64; SEQ ID NO:65; SEQ ID NO:66; SEQ ID NO:67; SEQ ID NO:68; SEQ ID NO:69; SEQ ID NO:70; SEQ ID NO:71; SEQ ID NO:72; SEQ ID NO:73; SEQ ID NO:74; SEQ ID NO:75; SEQ ID NO:76; SEQ ID NO:77; SEQ ID NO:78; SEQ ID NO:79; SEQ ID NO:80; SEQ ID NO:81; SEQ ID NO:82; SEQ ID NO:83; SEQ ID NO:84; SEQ ID NO:85; SEQ ID NO:86; SEQ ID NO:87; SEQ ID NO:88; SEQ ID NO:89; SEQ ID NO:90; SEQ ID NO:91; SEQ ID NO:92; SEQ ID NO:93; SEQ ID NO:94; SEQ ID NO:95; SEQ ID NO:96; SEQ ID NO:97; SEQ ID NO:98; SEQ ID NO:99; SEQ ID NO:100; SEQ ID NO:101; SEQ ID NO:102; SEQ ID NO:103; SEQ ID NO:104; SEQ ID NO:105; SEQ ID NO:106; SEQ ID NO:107; SEQ ID NO:108; SEQ ID NO:109; SEQ ID NO:110; SEQ ID NO:111; SEQ ID NO:112; SEQ ID NO:113; SEQ ID NO:114; SEQ ID NO:115; SEQ ID NO:116; SEQ ID NO:117; SEQ ID NO:118 and SEQ ID NO:119.

15 9. A nucleic acid molecule comprising a DNA sequence encoding the EPO receptor agonist polypeptide of claim 4.

20 10. A method of producing a EPO receptor agonist polypeptide comprising: growing under suitable nutrient conditions, a host cell transformed or transfected with a replicable vector comprising said nucleic acid molecule of claim 5, 6, 7, 8 or 9

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in a manner allowing expression of said EPO receptor agonist polypeptide and recovering said EPO receptor agonist polypeptide.

5 11. A composition comprising; a EPO receptor agonist polypeptide according to claim 1, 2, 3 or 4; and a pharmaceutically acceptable carrier.

10 12. A composition comprising; a EPO receptor agonist polypeptide according to claim 1, 2, 3 or 4; a factor; and a pharmaceutically acceptable carrier.

15 13. The composition of claim 12 wherein said factor is selected from the group consisting of: GM-CSF, G-CSF, c-mpl ligand, M-CSF, IL-1, IL-4, IL-2, IL-3, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-15, LIF, flt3/flk2 ligand, human growth hormone, B-cell growth factor, B-cell differentiation factor, eosinophil differentiation factor and stem cell factor, IL-3 variants, fusion proteins, G-CSF receptor agonists, c-mpl receptor agonists, IL-3 receptor agonists, multi-functional receptor agonists.

25 14. A method of stimulating the production of hematopoietic cells in a patient comprising the step of; administering a EPO receptor agonist polypeptide of claim 1, 2, 3 or 4, to said patient.

30 15. A method for selective ex vivo expansion of erythroid progenitors, comprising the steps of;

(a) culturing erythroid progenitor cells in a culture medium, comprising; a polypeptide of claim 1, 2, 3 or 4; and

35 (b) harvesting said cultured cells.

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16. A method for selective ex vivo expansion of erythroid progenitors, comprising the steps of;

(a) separating erythroid progenitor cells from other cells;

5 (b) culturing said separated erythroid progenitor cells with a selected culture medium comprising a polypeptide of claim 1, 2, 3 or 4; and

(c) harvesting said cultured cells.

10 17. A method for treatment of a patient having a hematopoietic disorder, comprising the steps of;

(a) removing erythroid progenitor cells;

(b) culturing said erythroid progenitor cells in a culture medium, comprising; a polypeptide of claim
15 1, 2, 3 or 4;

(c) harvesting said cultured cells; and

(d) transplanting said cultured cells into said patient.

20 18. A method for treatment of a patient having a hematopoietic disorder, comprising the steps of;

(a) removing erythroid progenitor cells;

(b) separating erythroid progenitor cells from other cells;

25 (c) culturing said separated erythroid progenitor cells with a selected culture medium comprising a polypeptide of claim 1, 2, 3 or 4;

(d) harvesting said cultured cells; and

(e) transplanting said cultured cells into said
30 patient.

19. A method of claim 15 wherein said erythroid progenitor cells are isolated from peripheral blood.

35 20. A method of claim 16 wherein said erythroid progenitor cells are isolated from peripheral blood.

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21. A method of claim 17 wherein said erythroid progenitor cells are isolated from peripheral blood.

22. A method of claim 18 wherein said erythroid
5 progenitor cells are isolated from peripheral blood.

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